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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,728	07/03/2001	John F. Wironen	RTI-133	8170

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,728	WIRONEN ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-23,31 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-23,31 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 1/23/06, has been entered.

Amended claims 1, 3, 4, 12-14, 19-20, and 22-23, filed 1/23/06, are acknowledged.

Claims herein under examination are 1, 3-23, 31, and 37.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-23, 31, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER

The following phrase does not appear to have written support in the specification, claims, or drawings, as originally filed: "tissue growth factor (TGF)" (instant claims 1 (line 9) and 23

(line 7)). While the specification recites "tissue growth factors" (page 21, line 23), the acronym TGF is assigned to "*transformation* growth factor" (page 2, second paragraph) not "*tissue* growth factors" which differs in scope. Because the introduction of "tissue growth factor (TGF)" does not appear to have adequate written support in the specification, claims, or drawings, as originally filed, this phrase with accompanying acronym is considered to be NEW MATTER. Claims 3-22, 31, and 37 are also rejected due to their direct or indirect dependency from claim 1.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-22, 31, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 1 recites the phrase "like implant materials comprising bone" (line 5) which is indefinite because it is unclear what is the intended meaning of "like" implant materials comprising bone. Does this mean they are all "like" bone? It is possible that Applicant intends the phrase to mean that the materials are "alike"; however, this is not clear. Claims 3-22, 31, and 37 are also rejected due to their direct or indirect dependency from instant claim 1.

Applicants argue that they have deleted the "like" reference to render the rejection moot. It is acknowledged that the term "like" has been deleted from line 2, but it remains in line 5 of instant claim 1.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 19-20, 22-23, 31, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (Journal of Periodontology, 1997 Nov; Vol. 68(11), pages 1076-1084).

Zhang et al. disclose an *in vitro* method for quantifying the osteoinductive potential of demineralized bone matrix (DBM), which is a collection of implant material containing bone morphogenetic proteins (BMPs) and other noncollagenous proteins, from cadaverous humans before clinical (human) use (allograft) (title; abstract; page 1077, col. 2, second and third paragraphs), as stated in instant claims 1, 3, and 23. Zhang et al. disclose the DBM is processed from ground bone (page 1077, first column, last paragraph to second column, first line) which represents cortical bone, cancellous bone, or a combination thereof, as stated in instant claim 3. Zhang et al. disclose osteoinductivity of demineralized bone matrix is due to bone morphogenetic proteins (BMPs) and other noncollagenous proteins in the matrix (page 1077, col. 1, third paragraph). Zhang et al. disclose exposing ground bone (implant material) to dilute hydrochloric acid, a demineralization process to dissolve the bone material (page 1077, col. 1,

last paragraph to col. 2, first paragraph) which represents the releasing step of instant claims 1, 4, and 5. Zhang et al. disclose calcium content of bone being demineralized can be demonstrated to be a linear function of pH of the solution (abstract and page 1077, col. 2, first paragraph) as well as calcium content determination (page 1077, col. 2, last paragraph to page 1078, col. 1, first paragraph) with the positive presence of calcium (abstract and Figures 1, 3, 4). Figure 3 shows calcium content less than 3%, as stated in instant claim 4. Zhang et al. disclose the bone matrices being separated into particles according to size ranges with sieves (page 1077, col. 1, last paragraph). Zhang et al. disclose combining bone cells with EDTA and trypsin (enzyme) (page 1078, col. 1, third paragraph) which represents dissolving the bone implant matrix with an enzyme, as stated in instant claims 5 and 6. Trypsin is utilized and then ALP was measured (page 1078, col. 2, first paragraph) which represents an enzyme that did not destroy osteoinductive factors present in the releasate, as stated in instant claim 6. Zhang et al. disclose quantifying the concentration of alkaline phosphatase (ALP) (implant material releasant of osteogenic factor) via a protein assay using milligram quantities (page 1078, col. 1, last paragraph to col. 2, first paragraph) and studying changes in ALP level with time to assess effects of DBM on human periosteal cell induction using 5 mg of DBM (which contains BMPs) per flask (page 1081, col. 1, second paragraph), which represents quantifying a concentration of at least one osteogenic factor present in an implant releasate, including BMPs, as stated in instant claims 1, 19, and 23. It is noted that that the limitation in instant claims 1 and 23 that states "does not require implantation of said materials *in vivo* or use of a living biological entity" is reasonably interpreted as not requiring but not necessarily excluding *in vivo* material or a living biological entity. Zhang et al. disclose mesenchymal cell induction process (morphogenic) is

frequently monitored by changes in ALP activity of cells being studied (page 1081, col. 1, second paragraph). Zhang et al. disclose noting changes in ALP concentration on curves with noted values of DBM (with BMPs) to determine osteogenic potential of implant material (Figures 6 and 7) which represents converting concentration values of an osteogenic factor to an osteogenic potential for a representative sampling whereby the osteogenic potential is realized, as stated in instant claims 1 and 23. The control curve in Figure 6 represents a predetermined curve, as stated in instant claims 1 and 23. Zhang et al. disclose proliferation effects of demineralized bone matrix were studied to assess potential mitogenic effects (page 1080, col. 2, second paragraph). Zhang et al. disclose a correlation graph between *in vitro* ALP activity (concentration) and percent calcium (probability to generate bone *in vivo*) (Figure 8), as stated in instant claim 20. Zhang et al. disclose using periosteal cells that are presumed to be responsive to BMPs actions, differentiating into osteoblast cells and correlations with ALP (Figure 8 and page 1083, col. 1, third and fourth paragraphs), as stated in instant claim 22. Zhang et al. disclose the *in vitro* assay may be a good substitute for the *in vivo* assay in assessing osteoinductive potential of demineralized bone matrix and reducing animal use via quality assessment of produced bone products (select bone material) for clinical application (to be implanted into patient) (page 1083, col. 1, last paragraph to col. 2, first paragraph), as stated in instant claim 31. Zhang et al. disclose that *in vitro* ALP activity peaks on day 5 and the *in vitro* assay requires only 1 week to obtain information regarding osteoinductive potential of demineralized bone products (page 1083, col. 2) which represents a total time of less than about 4 days with the word "about" being interpreted broadly, as stated in instant claim 37. Zhang et

al. disclose calcium contents are used as a major indicator of osteoinductivity (page 1082, col. 2, third paragraph) and Figure 8 demonstrates correlations between calcium and ALP (*in vitro*).

Thus, Zhang et al. anticipate the limitations in claims 1, 3-6, 19-20, 22-23, 31, and 37.

Applicants argue that Zhang et al. use *in vitro* assays and require living cells, whereas the instant invention "does not use a living biological entity". This statement is found unpersuasive as instant claims 1 and 23 recite "quantifying occurs *in vitro* and does not require implantation of said materials *in vivo* or use of a living biological entity" which is interpreted to mean that while the use of a living biological entity is not required, it is not prohibited from use in the invention. Applicants argue that the *in vitro* assay of Zhang et al. requires the use of cells, while Applicants' in vitro assay does not require the use of cells. It is noted that the instant claims do not prohibit the use of cells. Not requiring use and prohibiting use are very different issues and do not mean the same thing. Applicants argue that instant claims 1 and 23 now recite a Markush group of osteogenic factors which are analytes of the invention's *in vitro* assay and state that alkaline phosphatase (ALP) is not one of those analytes. It is noted that the Zhang et al. studies of ALP were performed with DBM which contains BMPs which are osteogenic factors found in the Markush group. Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 6, 2006

Carolyn Smith
Examiner
Art Unit 1631